Exhibit 20

WORLD HEALTH ORGANIZATION

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

IARC MONOGRAPHS
ON THE
EVALUATION OF THE CARCINOGENIC RISK OF CHEMICALS TO HUMANS

Some *N*-Nitroso Compounds

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EVALUATION OF THE CARCINOGENIC RISK

OF CHEMICALS TO HUMANS:

Some *N*-Nitroso Compounds

Volume 17

This publication represents the views and expert opinions
of an IARC Working Group on the
Evaluation of the Carcinogenic Risk of Chemicals to Humans
which met in Lyon,
10-15 October 1977

May, 1978

3.3 Case reports and epidemiological studies

No data were available to the Working Group.

4. Summary of Data Reported and Evaluation

4.1 Experimental data

N-Nitrosodiethylamine is carcinogenic in all animal species tested: mice, rats, Syrian golden, Chinese and European hamsters, guinea-pigs, rabbits, dogs, gerbils, pigs, monkeys, hedgehogs, various fish, frogs and birds. It induces benign and malignant tumours after its administration by various routes, including ingestion, parenteral injection, inhalation and rectal instillation. The major target organs are the liver, respiratory and upper digestive tracts and kidney. It is carcinogenic following its administration prenatally and in single doses. In several studies, dose-response relationships were established.

N-Nitroso-*N*-ethyl-*N*-(2-hydroxyethyl)amine, a metabolite of *N*-nitrosodiethylamine, produced mainly liver tumours after its oral administration to rats.

4.2 Human data

No case reports or epidemiological studies were available to the Working Group. Available information on occurrence suggests that the general population may be exposed to low levels of *N*-nitrosodiethylamine; however, no exposed group suitable for an epidemiological investigation has yet been identified.

4.3 Evaluation

There is *sufficient evidence* of a carcinogenic effect of *N*-nitrosodiethylamine in many experimental animal species. Although no epidemiological data were available, *N*-nitrosodiethylamine should be regarded for practical purposes as if it were carcinogenic to humans.

(b) Humans

In 4 men, laboratory exposure to NDMA gave rise to acute liver necrosis which later developed into cirrhosis; in one case, the acute liver injury proved to be fatal (Barnes & Magee, 1954; Freund, 1937).

Studies *in vitro* suggest that NDMA is metabolized by human liver and lung *via* the same metabolic pathway as in other mammalian species (Harris *et al.*, 1977; Montesano & Magee, 1970).

3.3 Case reports and epidemiological studies

No data were available to the Working Group.

4. Summary of Data Reported and Evaluation

4.1 Experimental data

N-Nitrosodimethylamine is carcinogenic in all animal species tested: mice, rats, Syrian golden, Chinese and European hamsters, guinea-pigs, rabbits, ducks, mastomys, various fish, newts and frogs. It induces benign and malignant tumours following its administration by various routes, including ingestion and inhalation, in various organs in various species. It produces tumours, mainly of the liver, kidney and respiratory tract. It is carcinogenic following its administration prenatally and in single doses. In several studies, dose-response relationships were established.

4.2 Human data

No case reports or epidemiological studies were available to the Working Group. Available information on occurrence suggests that the general population may be exposed to low levels of *N*-nitrosodimethylamine; however, no exposed group suitable for an epidemiological investigation has yet been identified. Reports of relatively high levels in certain pesticide formulations and of occupational exposures that may have occurred in the manufacture and use of rocket fuels may permit the identification of exposed groups.

4.3 Evaluation

There is *sufficient evidence* of a carcinogenic effect of *N*-nitrosodimethylamine in many experimental animal species. Similarities in its metabolism by human and rodent tissues have been demonstrated. Although no epidemiological data were available (and efforts should be directed toward this end), *N*-nitrosodimethylamine should be regarded for practical purposes as if it were carcinogenic to humans.